1. Ultralente-like crystals, comprising:

a) a derivatized human insulin or derivatized human insulin analog formed by derivatizing human insulin or a human insulin analog with a saturated, straight-chain fatty acid having from 4 to 16 carbon atoms such that the fatty acid forms an amide bond with the ε-amino group of the B29-lysine of human insulin or a human insulin analog; and

b) a divalent metal cation.

A1

2. The crystals of Claim 1, wherein the derivatized human insulin is selected from the group consisting of B29-butanoyl-human insulin, B29-pentanoyl-human insulin, and B29-hexanoyl-human insulin.

3. An insoluble composition, comprising the crystals of Claim 1.

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5. Ultralente-like crystals, comprising:

a) a protein selected from the group consisting of insulin and insulin analogs;

b) a derivatized human insulin or derivatized human insulin analog formed by derivatizing human insulin or a human insulin analog with a saturated, straight-chain fatty acid having from 4 to 16 carbon atoms such that the fatty acid forms an amide bond with the ε-amino group of the B29-lysine of human insulin or a human insulin analog; and

A2

c) a divalent metal cation.

6. The crystals of Claim 5 , wherein the protein is human insulin.

7. The crystals of Claim 1, wherein the protein is a monomeric insulin analog.

9. The crystals of Claim 1, wherein the molar proportion of derivatized human insulin or derivatized human insulin analog is from 15% to 90% of the total protein.

10. The crystals of Claim 1, wherein the divalent metal cation is zinc, which is present at about 0.3 mole per mole of total protein to about 2 moles per mole of total protein.

11. An insoluble composition, comprising the crystals of Claim 5.

13. A pharmaceutical composition, comprising an insoluble phase and a solution phase, wherein the insoluble phase comprises the insoluble composition of Claim 3 or 11, and wherein the soluble phase comprises an aqueous solvent.

14. The pharmaceutical composition of Claim 13 wherein the solution phase further comprises a preservative at a concentration of about 0.5 mg per mL to about 6 mg per mL of solution, a pharmaceutically acceptable buffer, and an isotonicity agent.

15. A method of treating diabetes comprising administering the crystals of Claim 1 or 5 to a patient in need thereof in a quantity sufficient to regulate blood glucose levels in the patient.

16. A method of treating diabetes comprising administering the insoluble composition of Claim 3 or 11 to a patient in need thereof in a quantity sufficient to regulate blood glucose levels in the patient.

17. A method of treating hyperglycemia comprising administering the crystals of Claim 1 or 5 to a patient in need thereof in a quantity sufficient to regulate blood glucose levels in the patient.

Q4 cont

18. A method of treating hyperglycemia comprising administering the insoluble composition of Claim 3 or 11 to a patient in need thereof in a quantity sufficient to regulate blood glucose levels in the patient.

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19. A process for preparing the crystals of Claim 1, comprising:

a) preparing a crystallization solution comprising the derivatized human insulin or derivatized human insulin analog, a buffer, a salt, and a divalent cation; and

b) allowing time for crystallization to occur.

20. A process for preparing the crystals of Claim 5, comprising:

a) preparing a crystallization solution comprising (i) a protein, (ii) a derivatized human insulin or derivatized human insulin analog, (iii) a buffer, (iv) a salt, and (v) a divalent cation;

b) combining the crystallization solution of a) with a nucleating seed suspension; and

c) allowing time for crystallization to occur.

Add new claims 21-28.

Q5

--21. The crystals of Claim 1, wherein the fatty acid is myristoyl fatty acid.

22. The crystals of Claim 1, wherein the fatty acid is n-octanoic fatty acid.

23. The crystals of claim 1, wherein the human insulin analog is des(ThrB30)-human insulin.

Q5 cont

24. The crystals of Claim 5, wherein the fatty acid is myristoyl fatty acid.

25. The crystals of claim 5, wherein the fatty acid is n-octanoic fatty acid.

26. The crystals of claim 5, wherein the human insulin analog is des(ThrB30)-human insulin.

27. The crystals of Claim 5, wherein the molar proportion of derivatized human insulin or derivatized human insulin analog is from 15% to 90% of the total protein.

28. The crystals of Claim 5, wherein the divalent metal cation is zinc, which is present at about 0.3 mole per mole of total protein to about 2 moles per mole of total protein.--

Remarks

I. Status Of The Claims

Claims 1-7 and 9-28 are active in this application.

II. Support For The Amendment

Support for the amendment of claims 1 and 5 is found in the specification, for example, at page 8, second full paragraph, and at page 12, first full paragraph.